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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/505,257	08/20/2004	Richard J Budhu	21044P	3816

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MERCK AND CO., INC
P O BOX 2000
RAHWAY, NJ 07065-0907

EXAMINER

CHU, YONG LIANG

ART UNIT PAPER NUMBER

1626

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/31/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary

Application No.:

10/505,257

Applicant(s)

BUDHU ET AL.

Examiner

Yong Chu

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 December 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4,6-17,28 and 29 is/are pending in the application.
- 4a) Of the above claim(s) 7,12,13,16,17 and 28 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4,6,8-11,14,15 and 29 is/are rejected.
- 7) ☒ Claim(s) 1-4,6,8-11,14,15 and 29 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input checked="" type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>5/6/2005 and 10/15/2004</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 5 and 18-27 are cancelled by amendment filed on 14 December 2006.

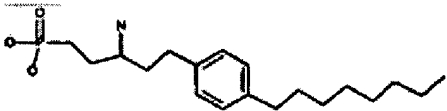
Claim 1, 8, and 9 are amended by the amendment. Therefore, claims 1-4, 6-17, 28, and 29 are pending in the instant application.

Information Disclosure Statement

Applicants' Information Disclosure Statements, filed on 6 May 2005 and 15 October 2004 have been considered. Please refer to Applicant's copies of the PTO-1449 submitted herewith.

Response to Lack of Unity

Applicants' election with traverse of Group I (claims 1-15, and 29) with elected

species of Example 3  for initial search purpose in the reply filed on 14 December 2006 is acknowledged. The traversal on the ground(s) that the claims satisfy the unity of invention requirement because the restricted groups are properly linked to form a single general inventive concept is not found persuasive. The structure of Formula I does not have a core structure, because there are many variables in the Formula (i.e. X, m, R₁-R₄, n, B). The specification fails to support the argument that all the claimed compounds possess the same utility as Edg receptor agonists. Therefore, the restriction requirement dated on 11/28/2006 is appropriate.

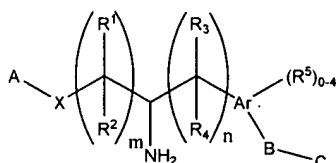
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Status of the Claims

Claims 16, 17, and 28 are withdrawn from further consideration by the Examiner as being drawn to non-elected inventions under 37 CFR 1.142(b) due to Restriction Requirement dated on 11/28/2006.

Elected Subject Matter

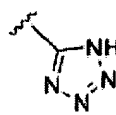
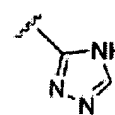
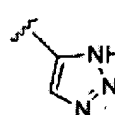
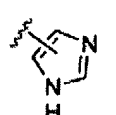
The scope of the invention of the elected subject matter is as follows:



Compounds of the Formula (I) or a pharmaceutically

acceptable salt or hydrate thereof, wherein:

Ar is phenyl; **m** is 1, 2, 3, or 4; **n** is 0, 1, 2, 3, or 4; **X** is a bond, O, or S(O)**k**, wherein **k** is 0, 1 or 2; **A** is selected from the group consisting of $-\text{CO}_2\text{H}$, $-\text{PO}_3\text{H}$, $-\text{PO}_2\text{H}_2$, $-\text{SO}_3\text{H}$,

$-\text{PO}(\text{R}^8)\text{OH}$,    ; **C** is not present; **B** is

$\text{C}_{5-16}\text{alkyl}$, $\text{C}_{5-16}\text{alkenyl}$ and $\text{C}_{5-16}\text{alkynyl}$; $(\text{R}^5)_{0-4}$ is $(\text{R}^5)_0$ as H; $\text{R}^1 - \text{R}^4$ is H or $\text{C}_{1-4}\text{alkyl}$;

R^8 is selected from the group consisting of: $\text{C}_{1-4}\text{alkyl}$ and aryl, wherein said $\text{C}_{1-4}\text{alkyl}$ is optionally substituted with 1-3 halo groups and aryl is optionally substituted with 1-5 substituents independently selected from the group consisting of: halo, $\text{C}_{1-6}\text{alkyl}$, $\text{C}_{3-6}\text{cycloalkyl}$, $\text{C}_{1-6}\text{alkoxy}$, $\text{C}_{1-4}\text{alkylthio}$ and $\text{C}_{3-6}\text{cycloalkoxy}$, said $\text{C}_{1-6}\text{alkyl}$, $\text{C}_{3-6}\text{cycloalkyl}$, $\text{C}_{1-6}\text{alkoxy}$, $\text{C}_{1-4}\text{alkylthio}$ and $\text{C}_{3-6}\text{cycloalkoxy}$ optionally substituted from one up to the maximum number of substitutable positions with halo,

As a result of the election and the corresponding scope of the invention identified supra, claims 7, 12, 13, and the remaining subject matter of claims 1-4, 6, 8-11, 14, 15, and 29 are withdrawn from further consideration pursuant to 37 CFR 1.142 (b) as being

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asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-4, 6, 8-11, 14, 15, and 29 are rejected under 35 U.S.C. 103(a) as being obvious over U.S. Patent No. 6,437,165 (Mandala et al.).

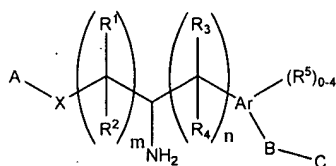
The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject

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matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Claims 1-4, 6, 8-11, 14, 15, and 29 are rejected under 35 U.S.C. 103 (a) as unpatentable over Mandala et al. U.S. Patent 6,437,165.

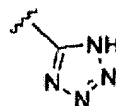
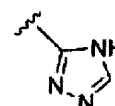
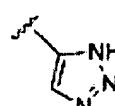

Applicant's instantly elected invention in claims 1-4, 6, 8-11, 14, 15, and 29 teach



compounds of formula (I)

pharmaceutically acceptable salts and pharmaceutical composition thereof wherein:

Ar is phenyl; **m** is 1, 2, 3, or 4; **n** is 0, 1, 2, 3, or 4; **X** is a bond, O, or S(O)**k**, wherein **k** is 0, 1 or 2; **A** is selected from the group consisting of -CO₂H, -PO₃H, -PO₂H₂, -SO₃H,

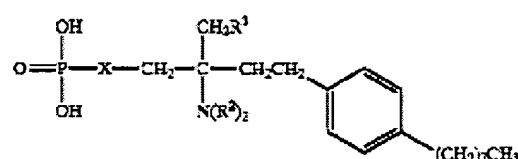
-PO(R⁸)OH,     ; **C** is not present; **B** is

C₅₋₁₆alkyl, C₅₋₁₆alkenyl and C₅₋₁₆alkynyl; (R⁵)₀₋₄ is (R⁵)₀ as H; R¹ - R⁴ is H or C₁₋₄alkyl;

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R⁸ is selected from the group consisting of: C₁₋₄alkyl and aryl, wherein said C₁₋₄alkyl is optionally substituted with 1-3 halo groups and aryl is optionally substituted with 1-5 substituents independently selected from the group consisting of: halo, C₁₋₆alkyl, C₃₋₆cycloalkyl, C₁₋₆alkoxy, C₁₋₄alkylthio and C₃₋₆cycloalkoxy, said C₁₋₆alkyl, C₃₋₆cycloalkyl, C₁₋₆alkoxy, C₁₋₄alkylthio and C₃₋₆cycloalkoxy optionally substituted from one up to the maximum number of substitutable positions with halo,

Determination of the scope and content of the prior art (MPEP §2141.01)



Mandala et al. teach specific compounds

Cpd	X	R ² /R ²	R ³
10	O	H/H	H
11	CH ₃	H/H	H
12	CH ₂ CH ₃	H/H	H

, and their pharmaceutical composition.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the prior art of Mandala et al. and the instantly claimed compounds, is that Mandala et al. teach the compounds with –CH₃ attached to the carbon next to the –NH₂, but does not teach the compounds with –H attached to the carbon next to the –NH₂ as in the instantly claimed compounds such as the first compound of claim 15.

Finding of prima facie obviousness--rational and motivation (MPEP §2142-2413)

One skilled in the art would have found the claimed compound prima facie obvious because it is well established that the substitution of methyl for hydrogen on a known compound is not a patentable modification absent unexpected or unobvious

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results. *In re Wood*, 199 U.S.P.Q. 137 (C.C.P.A. 1978) and *In re Lahr*, 137 U.S.P.Q. 548, 549 (C.C.P.A. 1963). The motivation to make the claimed compounds derives from the expectation that structurally similar compounds would possess similar activity (i.e pharmacological use). Because the compound claims are unpatentable, the composition claims comprising the said compound are unpatentable either.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

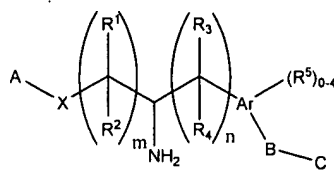
A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-4, 6, 8-11, 14, 15, and 29 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-11 of U.S. Patent No. 6,437,165. Although the conflicting claims are not identical, they are not patentably distinct from each other.

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Applicant's instantly elected invention in claims 1-4, 6, 8-11, 14, 15, and 29 teach

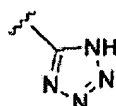
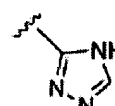
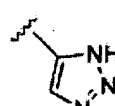



compounds of formula (I)

pharmaceutically acceptable salts and pharmaceutical composition thereof wherein:

Ar is phenyl; **m** is 1, 2, 3, or 4; **n** is 0, 1, 2, 3, or 4; **X** is a bond, O, or S(O)**k**, wherein **k** is

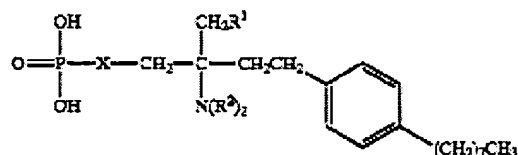
0, 1 or 2; **A** is selected from the group consisting of $-\text{CO}_2\text{H}$, $-\text{PO}_3\text{H}$, $-\text{PO}_2\text{H}_2$, $-\text{SO}_3\text{H}$,

$-\text{PO}(\text{R}^8)\text{OH}$,    ; **C** is not present; **B** is

$\text{C}_{5-16}\text{alkyl}$, $\text{C}_{5-16}\text{alkenyl}$ and $\text{C}_{5-16}\text{alkynyl}$; $(\text{R}^5)_{0-4}$ is $(\text{R}^5)_0$ as H; $\text{R}^1 - \text{R}^4$ is H or $\text{C}_{1-4}\text{alkyl}$;

R^8 is selected from the group consisting of: $\text{C}_{1-4}\text{alkyl}$ and aryl, wherein said $\text{C}_{1-4}\text{alkyl}$ is optionally substituted with 1-3 halo groups and aryl is optionally substituted with 1-5 substituents independently selected from the group consisting of: halo, $\text{C}_{1-6}\text{alkyl}$, $\text{C}_{3-6}\text{cycloalkyl}$, $\text{C}_{1-6}\text{alkoxy}$, $\text{C}_{1-4}\text{alkylthio}$ and $\text{C}_{3-6}\text{cycloalkoxy}$, said $\text{C}_{1-6}\text{alkyl}$, $\text{C}_{3-6}\text{cycloalkyl}$, $\text{C}_{1-6}\text{alkoxy}$, $\text{C}_{1-4}\text{alkylthio}$ and $\text{C}_{3-6}\text{cycloalkoxy}$ optionally substituted from one up to the maximum number of substitutable positions with halo,

Determination of the scope and content of the prior art (MPEP §2141.01)



Mandala et al. teach specific compounds

Cpd	X	R^2/R^3	R^1
10	O	H/H	H
11	CH_2	H/H	H
12	CH_2CH_3	H/H	H

, and their pharmaceutical composition.

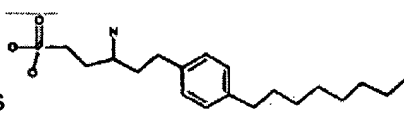
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drawn to non-elected inventions. The withdrawn compounds contain varying functional groups which are chemically recognized to differ in structure, function, and reactivity.

Therefore, claims 1-4, 6, 8-11, 14, 15, and 29 (in part) will be examined on the merits.

Specification

The disclosure is objected to because of the following informalities: The chemical formulae in page 18-21, and 27 are not complete. For example, substitutes for "N" are

missing from the formula, shown as  . Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-4, 6, 8-11, 14, 15, and 29 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible asserted utility or a well established utility.

The instant specification fails to disclose utility data to support the claim that the compounds of Formula (I) possess the utility as EDG receptor agonists and for treating diseases or condition mediated by that receptor.

Claims 1-4, 6, 8-11, 14, 15, and 29 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the prior art of Mandala et al. and the instantly claimed compounds, is that Mandala et al. teach the compounds with $-\text{CH}_3$ attached to the carbon next to the $-\text{NH}_2$, but does not teach the compounds with $-\text{H}$ attached to the carbon next to the $-\text{NH}_2$ as in the instantly claimed compounds such as the first compound of claim 15.

Finding of prima facie obviousness--rational and motivation (MPEP §2142-2413)

One skilled in the art would have found the claimed compound prima facie obvious because it is well established that the substitution of methyl for hydrogen on a known compound is not a patentable modification absent unexpected or unobvious results. In re Wood, 199 U.S.P.Q. 137 (C.C.P.A. 1978) and In re Lahr, 137 U.S.P.Q. 548, 549 (C.C.P.A. 1963). The motivation to make the claimed compounds derives from the expectation that structurally similar compounds would possess similar activity (i.e pharmacological use). Because the compound claims are unpatentable, the composition claims comprising the said compound are unpatentable either.

Claim Objections

Claims 1-4, 6, 8-11, 14, 15, and 29 are objected to for containing elected and non-elected subject matter. The elected subject matter has been identified supra.

Conclusion

- Claims 1-4, 6, 8-11, 14, 15, and 29 are objected.
- Claims 1-4, 6, 8-11, 14, 15, and 29 are rejected

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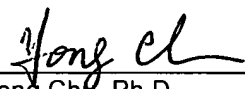
Telephone Inquiry

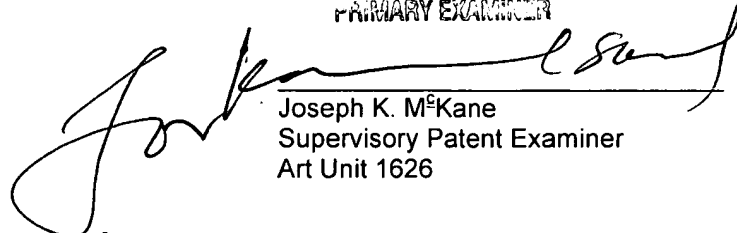
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Chu whose telephone number is 571-272-5759.

The examiner can normally be reached between 7:00 am - 3:30 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane can be reached on 571-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Yong Chu, Ph.D.
Patent Examiner
Art Unit 1626

MARCEL A. SASED, Ph.D.
PRIMARY EXAMINER

Joseph K. McKane
Supervisory Patent Examiner
Art Unit 1626